Renal Replacement Therapy in AKI

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Outlines

- Definition and Stage-Based Management of AKI
- Modality of RRT for patients with AKI
- Initiation and Goals of RRT
- Early vs Late Initiation of RRT in AKI
- Dose of RRT in AKI
- When to Stop RRT in AKI
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- Dialyzer membranes for RRT in AKI
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Definition

RIFLE and AKIN Criteria for Diagnosis and Classification of AKI

RIFLE			AKIN	
Class	SCr[a]	Urine Output (common to both)	Stage	SCr[b]
Risk	Increased SCr to >1.5× baseline	Urine output <0.5 mg/kg/h for >6 h	1	Increase in SCr ≥0.3 mg/dL or increase in SCr to ≥150%-200% of baseline
Injury	Increased SCr to >2× baseline	Urine output <0.5 mg/kg/h for >12 h	2	Increase in SCr to >200%-300% of baseline
Failure	Increased SCr to >3× baseline; or an increase of ≥0.5 mg/dL to a value of ≥4 mg/dL	Urine output <0.3 mg/kg/h for >12 h or anuria for >12 h	3	Increase in SCr to >300% of baseline; or to ≥4 mg/dL with an acute increase of ≥0.5 mg/dL; or on RRT
Loss	Need for RRT for >4 wk			
End Stage	Need for RRT for >3 mo			

Abbreviations: AKI, acute kidney injury; AKIN, Acute Kidney Injury Network; RIFLE, risk, injury, failure, loss, end-stage disease; RRT, renal replacement therapy; SCr, serum creatinine.

[a]For RIFLE, the increase in SCr should be both abrupt (within 1-7 days) and sustained (>24 hours).

[b]For AKIN, the increase in SCr must occur in less than 48 hours.

Definition

Summary of KDIGO Recommendation Statements: Definition of AKI.

2.1.1: AKI is defined as any of the following (*Not Graded*):

- Increase in SCr by ≥0.3 mg/dL (≥26.5 μmol/L) within 48 hours; or
- Increase in SCr to ≥1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or
- Urine volume <0.5 mL/kg/h for 6 hours.

Stage-Based Management of AKI

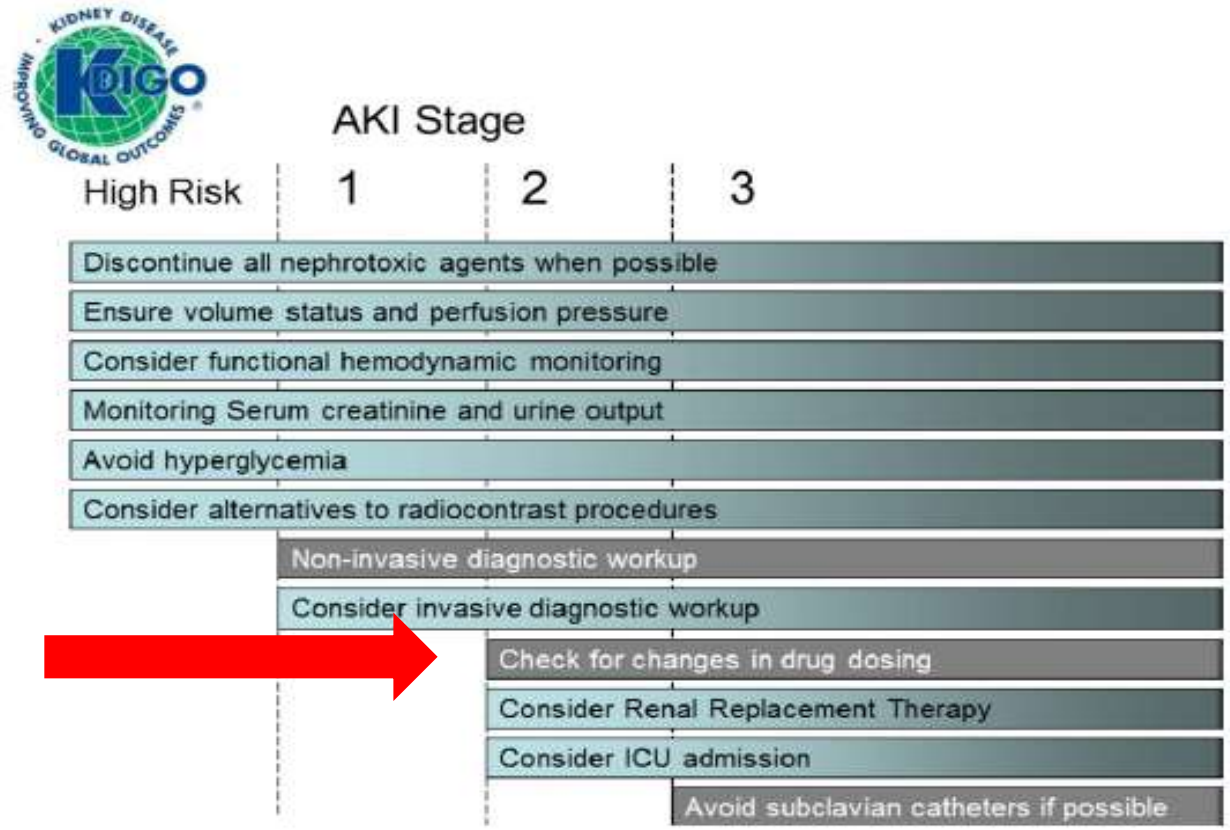
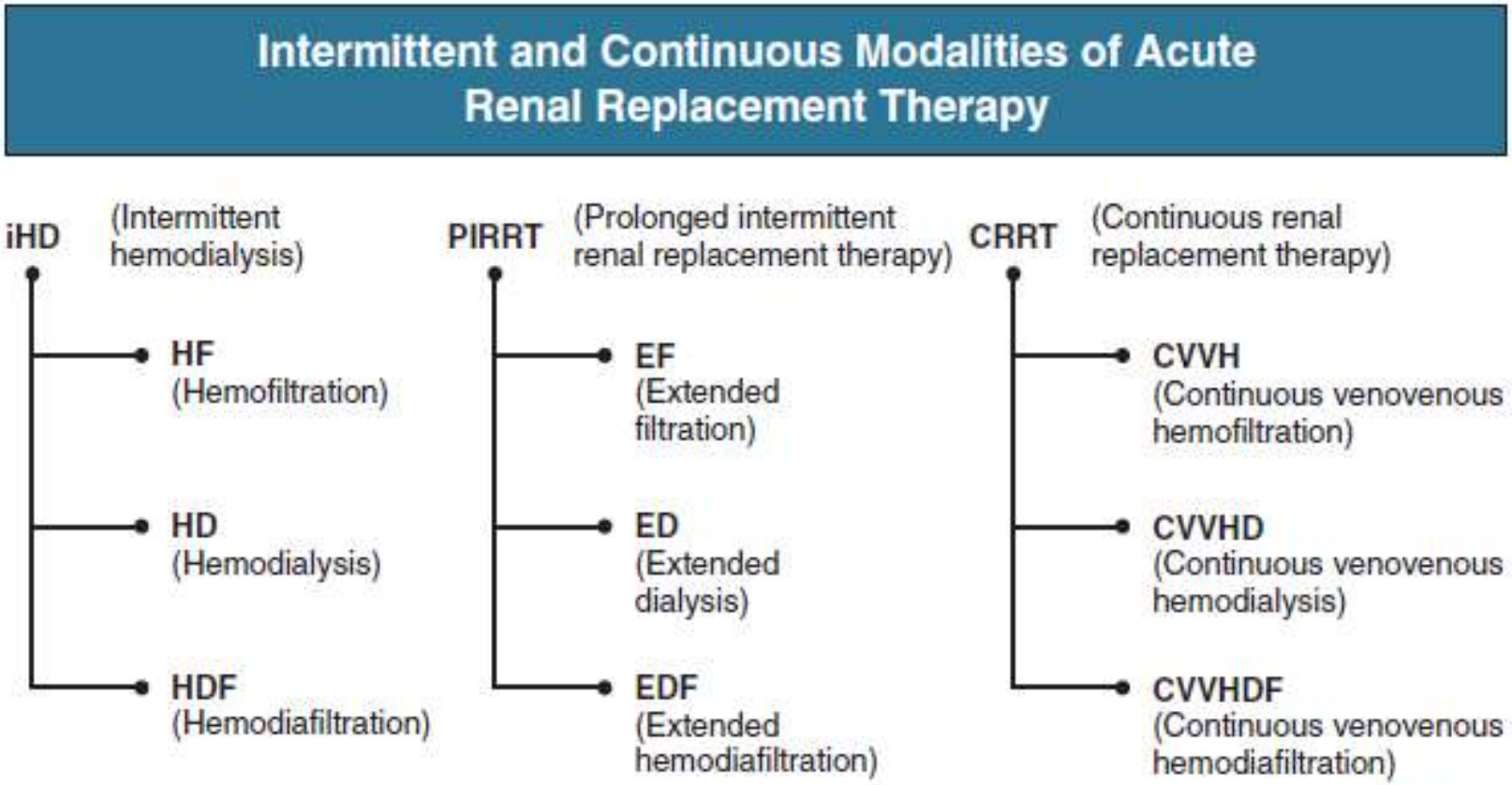


Figure 2. Stage-based management of acute kidney injury (AKI). Shading of boxes indicates priority of action—solid shading (with white lettering) indicates actions that are equally appropriate at all stages whereas graded shading (with black lettering) indicates increasing priority as intensity increases. Abbreviation: ICU, intensive care unit. Reproduced with permission of KDIGO from the *KDIGO Clinical Practice Guideline for Acute Kidney Injury*.[1]

Modality of renal replacement therapy for patients with AKI



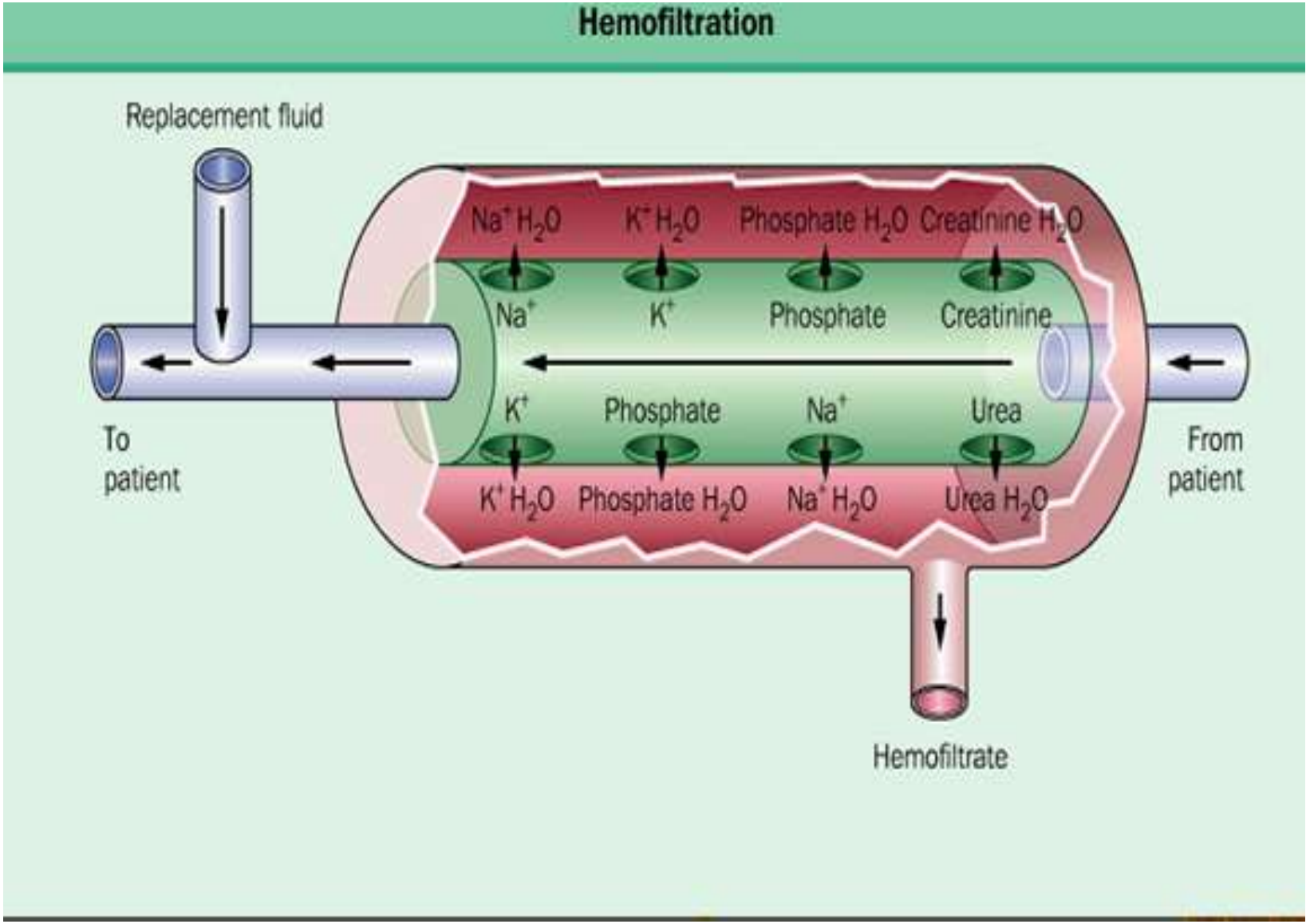
Intermittent and continuous modalities of acute renal replacement therapy. *(Adapted from reference 40.)*

Current Modalities of RRT for Patients with AKI

Typical setting of different RRT modalities for AKI (for 70-kg patient)

	SCUF	CVVH	CVVHD	CVVHDF	SLED	IHD
Blood flow (ml/min)	100–200	150–250	150–250	150–250	100–300	200–300
Predominant solute transport principle	convection	convection	diffusion	diffusion + convection	diffusion	diffusion
Ultrafiltrate (ml/h)	100–300	1500–2000	variable	1000–1500	variable	variable
Dialysate flow (ml/h)	0	0	1500–2000	1000–1500	100–300 ml/min	300–500 ml/min
Effluent volume (l/d)	2–8	36–48	36–48	36–72	N/A	N/A
Replacement fluid for zero balance (ml/h)	0	1500–2000	0	1000–1500	0	0
Urea clearance (ml/min)	1–5	25–33	25–33	25–33	80–90	variable

CVVH, continuous venovenous hemofiltration; CVVHD, continuous venovenous hemodialysis, CVVHDF, continuous venovenous hemodialfiltration; IHD, intermittent hemodialysis; N/A, not applicable; PD, peritoneal dialysis; SCUF, slow continuous ultrafiltration; SLED, slow low-efficiency dialysis.


Hemofiltration
Replacement fluid
Na⁺ H₂O
K⁺ H₂O
Phosphate H₂O
Creatinine H₂O
Na⁺
K⁺
Phosphate
Creatinine
K⁺
Phosphate
Na⁺
Urea
To patient
From patient
K⁺ H₂O
Phosphate H₂O
Na⁺ H₂O
Urea H₂O
Hemofiltrate

CRRT

The advantages of CRRT over IHD are:

The slower fluid removal, resulting in more hemodynamic stability and better control of fluid balance, *the slower control of solute concentration*, *avoiding large fluctuations and fluid shifts* (including a reduced risk [worsening] of cerebral edema), *the great flexibility* (allowing adaptation of the treatment to the patient's need at any time), and *the ability to perform the treatment with relatively simple and user-friendly machines* (allowing ICU nurses to monitor the treatment).

Disadvantages include the need for:

Immobilization, *the use of continuous anticoagulation*, *the risk of hypothermia and higher costs*.

IHD

Major advantages of IHD over CRRT are :

The fast removal of toxins and the restricted treatment period, allowing down-time for diagnostic and therapeutic interventions.

IHD may, therefore, be the preferred treatment in patients where immediate removal of small solutes is required, such as severe hyperkalemia, some cases of poisoning, and tumor lysis syndrome.

Hybrid treatments, such as SLED, may share some of the advantages of both IHD and CRRT without having their disadvantages.

Theoretical advantages and disadvantages of CRRT, IHD, SLED, and PD

Modality	Potential setting in AKI	Advantages	Disadvantages
IHD	Hemodynamically stable	Rapid removal of toxins and low-molecular-weight substances Allows for "down time" for diagnostic and therapeutic procedures Reduced exposure to anticoagulation Lower costs than CRRT	Hypotension with rapid fluid removal Dialysis disequilibrium with risk of cerebral edema Technically more complex and demanding
CRRT	Hemodynamically unstable Patients at risk of increased intracranial pressure	Continuous removal of toxins Hemodynamic stability Easy control of fluid balance No treatment-induced increase of intracranial pressure User-friendly machines	Slower clearance of toxins Need for prolonged anticoagulation Patient immobilization Hypothermia Increased costs
SLED	Hemodynamically unstable	Slower volume and solute removal Hemodynamic stability Allows for "down time" for diagnostic and therapeutic procedures Reduced exposure to anticoagulation	Slower clearance of toxins Technically more complex and demanding

Modality of renal replacement therapy for patients with AKI

5.6.2: We suggest using CRRT, rather than standard intermittent RRT, for hemodynamically unstable patients. (2B)

In *conclusion*, in the presence of hemodynamic instability in patients with AKI, CRRT is preferable to standard IHD.

SLED may also be tolerated in hemodynamically unstable patients with AKI in settings where other forms of CRRT are not available, but data on comparative efficacy and harm are limited.

Once hemodynamic stability is achieved, treatment may be switched to standard IHD.

Modality of renal replacement therapy for patients with AKI

5.6.3: We suggest using **CRRT**, rather than **intermittent RRT**, for AKI patients with ***acute brain injury*** or other causes of increased intracranial pressure or generalized brain edema. (2B)

In a patient with ***acute brain injury***, IHD may worsen neurological status by compromising cerebral perfusion pressure.

- This may be the result of a decrease of mean arterial pressure (dialysis-induced hypotension) or an increase of cerebral edema and intracranial pressure (dialysis disequilibrium), and may jeopardize the potential for neurologic recovery.

Initiation of RRT

5.1.1: Initiate RRT emergently when ***life-threatening*** changes in fluid, electrolyte, and acid-base balance exist. (Not Graded)

5.1.2: Consider the ***broader clinical context***, the presence of conditions that can be modified with RRT, and ***trends*** of laboratory tests—rather than single BUN and creatinine thresholds alone—when making the decision to start RRT. (Not Graded)

Initiation of RRT

- While no RCTs exist for dialysis for life-threatening indications, it is widely accepted that patients with ***severe hyperkalemia, severe acidosis, pulmonary edema, and uremic complications*** should be dialyzed emergently.

- A variety of ***poisons, drug overdoses, and toxic compounds*** (e.g., salicylates, ethylene glycol, methanol, metformin) can contribute to acid-base problems and also lead to AKI.

  In these circumstances, RRT may also facilitate removal of the offending drug.

Goals of Renal Replacement Therapy

i) Maintain fluid and electrolyte, acid-base, and solute homeostasis

ii) To permit renal recovery and to prevent further insults to the kidney

iii) To allow other supportive measures (e.g., antibiotics, nutrition support) to proceed without limitation or complication.

Ideally, therapeutic interventions should be designed to achieve the above goals and a systematic assessment of all these factors is key to determining the optimal timing for initiating dialysis.

Early vs Late Initiation of RRT in AKI

- Only ***one RCT*** has evaluated the effect of timing of initiation of RRT on outcome.
- ***Bouman et al;*** randomized 106 critically ill patients with AKI to early vs. late initiation of RRT.
- ***The early initiation*** group started RRT within 12 hours of oliguria (<30 ml/h for 6 hours, not responding to diuretics or hemodynamic optimization), or CrCl < 20 ml/min.
- ***The late-initiation*** group started RRT when classic indications were met.
- The study ***did not find differences*** in ICU or hospital mortality, or in renal recovery among survivors, ***but was clearly too small to allow for definitive conclusions.***

Bouman CS, Oudemans-Van Straaten HM, Tijssen JG, Zandstra DF, Kesecioglu J. Crit Care Med 2002; 30: 2205–2211.
Department of Intensive Care, Academic Medical Center, Amsterdam, The Netherlands

Early vs Late Initiation of RRT in AKI

- A prospective multicenter observational cohort study performed by the ***Program to Improve Care in Acute Renal Disease (PICARD)*** analyzed dialysis initiation—as inferred by BUN concentration—in ***243*** patients from ***5*** geographically and ethnically diverse clinical sites.
- Adjusting for age, hepatic failure, sepsis,thrombocytopenia, and s.creatinine, and stratified by site and initial dialysis modality.
- ***Initiation of RRT at higher BUN (>76 mg/dl) was associated with an increased risk of death (RR 1.85; 95% CI 1.16 –2.96).***

Liu KD, et al. Timing of initiation of dialysis in critically ill patients with acute kidney injury.Clin J Am Soc Nephrol 2006; 1:915–919.

Early vs Late Initiation of RRT in AKI

Observational studies:

- Single-center observational studies that were restricted to AKI after trauma (HD) and coronary artery bypass surgery (CVVHDF, CVVH)
- **Early** starters: BUN 42 mg/dl, **Late** starters: BUN 92 mg/dl

  early starters – urine output is less than 100 mL/8 hours

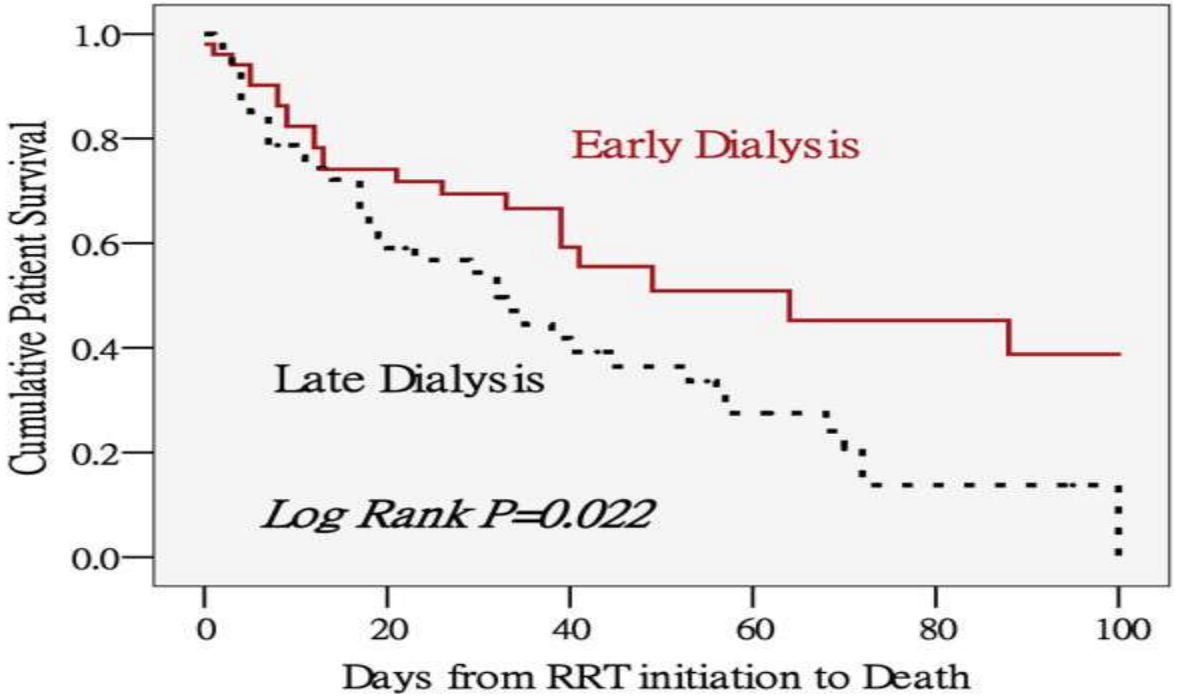
  time between the operation and the initiation
- **Conclusion**: Suggested a benefit "survival" to RRT initiation at early start "at lower BUN concentrations"

Gettings LG, Intensive Care Med 1999; 25: 805–813., Demirkilic U, J Card Surg 2004; 19: 17–20. Elahi MM, Eur J Cardiothorac Surg 2004; 26: 1027–1031.

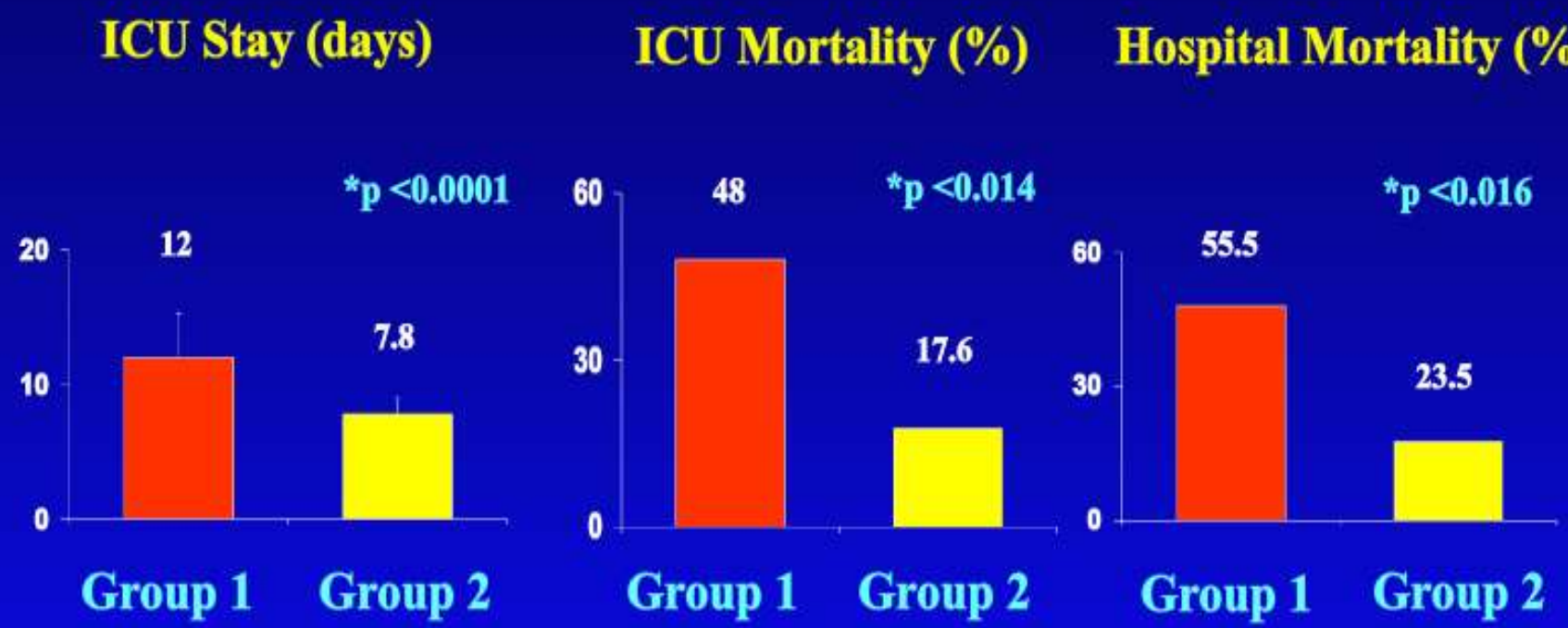
Early vs Late Initiation of RRT in AKI

Late initiation of renal replacement therapy is associated with worse outcomes in acute kidney injury after major abdominal surgery.

Shiao CC, et al. Crit Care 2009; 13: R171.



Early CRRT after Cardiac Surgery is Associated with Improved Survival- 1



Demirkilic et al. J Card Surg 19: 17, 2004

Early vs Late Initiation of RRT in AKI

- Observational studies:
  - A prospective multicenter observational study (54 ICUs in 23 countries)
    - Stratified into "early" or "late" by median urea at the time RRT started (145mg/dl)
      - Also categorized temporally from ICU admission into early "less than 2days", delayed "between 2–5 days", or late "more than 5 days".

Conclusion: timing by serum urea showed a tendency but no significant difference in mortality in relation to ICU admission, late RRT was associated with greater crude mortality

Bagshaw SM, et al. Timing of renal replacement therapy and clinical outcomes in critically ill patients with severe acute kidney injury. J Crit Care 2009; 24: 129–140.

Early vs Late Initiation of RRT in AKI

- *Traditional indications* for RRT, developed for patients with advanced CKD, are not necessarily valid in the context of AKI.
- *For instance*, massive volume overload resulting from volume resuscitation may be an indication for RRT even in the absence of significant elevations in BUN or SCr.
- *In this instance*, it may be more appropriate to consider dialytic intervention in the ICU patient as a form of renal support rather than renal replacement.
- *Indeed*, some of the traditional indications for dialysis (e.g., uremic pericarditis, pleuritis, encephalopathy, coagulopathy) would be considered ‘‘complications’’ of AKI rather than “indications” for RRT.

Dose of renal replacement therapy in AKI

5.8.1: The dose of RRT to be delivered should be prescribed before starting each session of RRT. (Not Graded)

We recommend frequent assessment of the actual delivered dose in order to adjust the prescription. (1B)

5.8.2: Provide RRT to achieve the goals of electrolyte, acid-base, solute, and fluid balance that will meet the patient's needs. (Not Graded)

5.8.3: We recommend delivering a Kt/V of 3.9 per week when using intermittent or extended RRT in AKI. (1A)

5.8.4: We recommend delivering an effluent volume of 20–25ml/kg/h for CRRT in AKI (1A).

This will usually require a higher prescription of effluent volume. (Not Graded)

When to Stop RRT in AKI

5.2.1: Discontinue RRT when it is **no longer required**, either because intrinsic kidney function has recovered to the point that it is adequate to meet patient needs, or because RRT is **no longer consistent** with the goals of care. (Not Graded)

More than 50% of patients with severe AKI will not improve, despite appropriate therapy. The incidence of withdrawal of life-support treatments in critically ill patients with multiorgan failure has increased over the last decade.

Prendergast TJ, Luce JM. Am J Respir Crit Care Med 1997

Anticoagulation

The goal of anticoagulation with RRT is to prevent clotting of the filter and/or reduction in membrane permeability, and thus to achieve adequate RRT and to prevent blood loss in the clotted filter.

These benefits have to be weighed against the risk of bleeding, and economic issues, such as workload and costs.

Patients with impaired coagulation (e.g: thrombocytopenia, or prolonged prothrombin time or activated partial thromboplastin time) due to underlying diseases such as liver failure or dilution coagulopathy, may not benefit from additional anticoagulation for RRT.

Anticoagulation

5.3.1: In a patient with AKI requiring RRT, base the decision to use anticoagulation for RRT on assessment of the patient's potential risks and benefits from anticoagulation.

(Not Graded)

5.3.1.1: We recommend using anticoagulation during RRT in AKI if a patient does not have an increased bleeding risk or impaired coagulation and is not already receiving systemic anticoagulation. (1B)

Anticoagulation

5.3.3: For patients with increased bleeding risk who are not receiving anticoagulation, we suggest the following for anticoagulation during RRT:

5.3.3.1: We suggest using regional citrate anticoagulation, rather than no anticoagulation, during CRRT in a patient without contraindications for citrate. (2C)

5.3.3.2: We suggest avoiding regional heparinization during CRRT in a patient with increased risk of bleeding. (2C)

Anticoagulation

5.3.4: In a patient with heparin-induced thrombocytopenia, all heparin must be stopped and we recommend using direct thrombin inhibitors (such as argatroban) or Factor Xa inhibitors (such as danaparoid or fondaparinux) rather than other or no anticoagulation during RRT. (1A)

5.3.4.1: In a patient with heparin-induced thrombocytopenia who does not have severe liver failure, we suggest using argatroban rather than other thrombin or Factor Xa inhibitors during RRT. (2C)

Vascular access for renal replacement therapy in AKI

A prerequisite for all ARRT modalities is reliable vascular access characterized by *low resistance to flow and minimal access recirculation*. AV fistulas and prosthetic bridge grafts should be used in patients who have them.

However, access is usually via uncuffed untunnelled (temporary) double-lumen catheters in the internal jugular, femoral veins, or less frequently subclavian catheters because they are associated with a higher incidence of procedural complications, venous stenosis, and thrombosis.

Left-sided internal jugular and subclavian catheters provide flows that are more erratic and up to 100 ml/min lower than elsewhere. Femoral and right-sided internal jugular or subclavian catheters provide the best *Qb.*

Vascular access for renal replacement therapy in AKI

Functional vascular access is essential for adequate RRT. Basic requirements are to ensure adequate and regular flow with low morbidity.

5.4.1: We suggest initiating RRT in patients with AKI via an **uncuffed nontunneled dialysis catheter**, rather than a tunneled catheter. (2D)

5.4.2: When choosing a vein for insertion of a dialysis catheter in patients with AKI, consider these preferences:

First choice: right jugular vein; **Second choice:** femoral vein; **Third choice:** left jugular vein; **Last choice:** subclavian vein with preference for the dominant side. (Not Graded)

Vascular access for renal replacement therapy in AKI

5.4.3: We recommend using ultrasound guidance for dialysis catheter insertion. (1A)

5.4.4: We recommend obtaining a chest radiograph promptly after placement and before first use of an internal jugular or subclavian dialysis catheter. (1B)

5.4.5: We suggest not using topical antibiotics over the skin insertion site of a nontunneled dialysis catheter in ICU patients with AKI requiring RRT. (2C)

5.4.6: We suggest not using antibiotic locks for prevention of catheter-related infections of nontunneled dialysis catheters in AKI requiring RRT. (2C)

Dialyzer membranes for RRT in AKI

Semipermeable hollow-fiber dialyzers are used as standard of care for both solute clearance and ultrafiltration in IHD and CRRT.

5.5.1: We suggest to use dialyzers with a biocompatible membrane for IHD and CRRT in patients with AKI. (2C)

Buffer solutions for renal replacement therapy in patients with AKI

One goal of CRRT is to maintain normal or near-normal acid-base balance, *thus preventing detrimental effects of acidosis on cardiovascular performance and hormonal response.*

Options for correction of metabolic acidosis include the use of acetate-, lactate-, and bicarbonate containing replacement solutions or dialysate.

The use of bicarbonate as a buffer in the dialysate or replacement fluid of AKI patients results in *better correction of acidosis, lower lactate levels, and improved hemodynamic tolerance.*

Buffer solutions for renal replacement therapy in patients with AKI

5.7.1: We suggest using ***bicarbonate***, rather than ***lactate***, as a buffer in dialysate and replacement fluid for RRT in patients with AKI. (2C)

5.7.2: We recommend using ***bicarbonate***, rather than ***lactate***, as a buffer in dialysate and replacement fluid for RRT in patients with AKI and circulatory shock. (1B)

5.7.3: We suggest using ***bicarbonate***, rather than ***lactate***, as a buffer in dialysate and replacement fluid for RRT in patients with AKI and liver failure and/or lactic acidemia. (2B)

Microbiological quality standards of different regulatory agencies

	ANSI/AAMI/ISO[763–765]	ERA-EDTA guidelines[765a]
Water for dialysis		
Bacteria (CFU/ml)	<100 (action level at 50)	<100
Endotoxin (EU/ml)	<0.5	<0.25
Dialysate		
Bacteria (CFU/ml)	<100 (action level at 50)	<100
Endotoxin (EU/ml)	<0.5	<0.25
Ultrapure dialysate		
Bacteria (CFU/ml)	<0.1	<0.1
Endotoxin (EU/ml)	<0.03	<0.03
Substitution fluid for infusion		
Bacteria (CFU/ml)	Sterile	$<10^{-6}$
Endotoxin (EU/ml)	Undetectable	<0.03

AAMI, Association for the Advancement of Medical Instrumentation; ANSI, American National Standards Institute; CFU, colony-forming units; ERA-EDTA, European Renal Association—European Dialysis and Transplant Asssociation; EU, endotoxin units; ISO, International Organization for Standardization.

5.7.4: We recommend that dialysis fluids and replacement fluids in patients with AKI, at a minimum, comply with American Association of Medical Instrumentation (AAMI) standards regarding contamination with bacteria and endotoxins. (1B)

Conclusion

As regard timing of RRT, calling for an adequately powered randomized controlled trial to address this question

No RRT is ideal for all patients with AKI.

Clinicians should be aware of the ***pros*** and ***cons*** of different RRTs, and tailor RRT on the basis of the individual and potentially changing needs of their patients.

Besides the individual patient's characteristics, the available expertise and resources may also be an important determinant of the ultimate choice.

THANK YOU

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